Ensuring Access to Innovative Therapies:
Discovery to Approved Product

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Pfizer Animal Health

Access to Innovative Therapies

- Discovery: Identifying the commercial need for novel compounds
- Developing & registering a marketable novel product
- Case example: Improvest
- Conclusion – the innovation paradox

Commercial Need for Novel Compounds

- The business of pioneer pharmaceutical companies is to identify medical needs that can be treated with novel compounds
- …then develop novel products from those compounds and demonstrate safety, efficacy, and product quality for the intended uses
- Return on R&D investment depends on:
  - Novelty
  - “Patentability”
  - Value in the marketplace

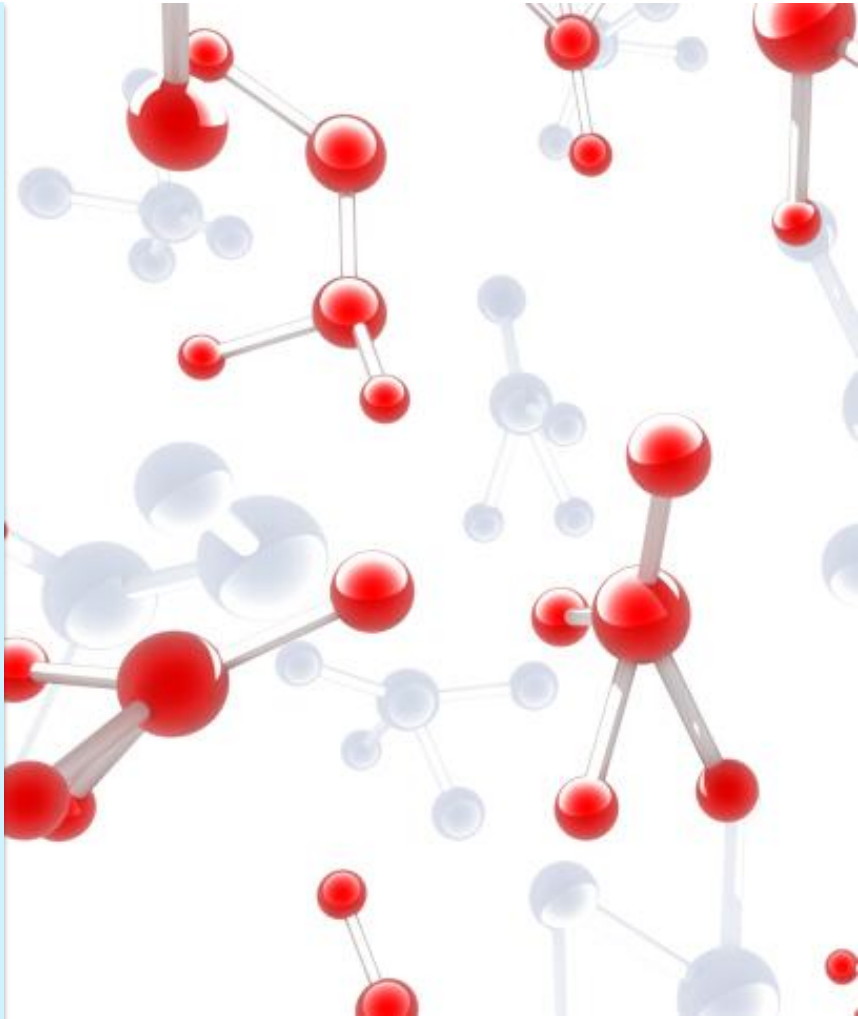
Commercial Need for Novel Compounds

Identifying Medical Needs

- What are the drivers for discovery of novel agents?
  - User needs (convenience, compliance, cures, cost)
  - Resistance to existing therapies
  - Regulatory framework
  - Consumer acceptance
- Predict the market's needs 8–12 years ahead!

AH Substrate Being Expanded to Include Novel Compounds

- Substantial decrease in human health antibiotics programs
  - Human health more focused on chronic use drugs / conditions
  - Less available substrate for leveraging
- Where can animal health antibiotics programs look for new substrate?
  - Traditional Small Molecules
    - Novel Antibacterial Classes
    - Re-exploration of older generations of existing classes
  - Novel Substrate
    - Antimicrobial peptides
    - Bacteriophages
    - Probiotics

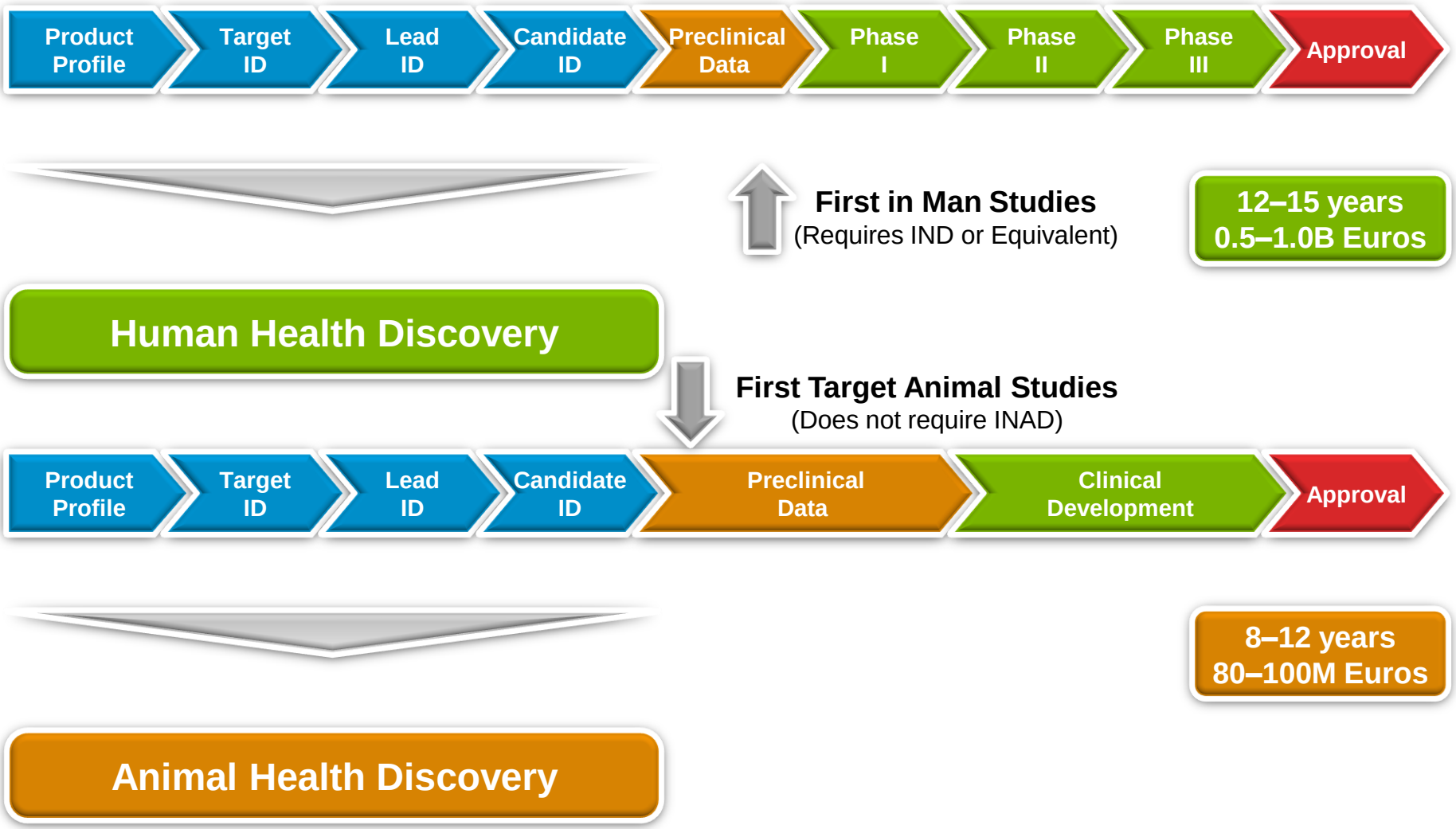


Getting Novel Compounds to the Marketplace

Developing Novel Products

- Commercial accessibility of novel compounds depends on
  - Successful new molecule discovery
  - Advancement of the drug candidate through clinical development
  - Formulation and chemistry
  - Validation of a commercial-scale manufacturing process
  - Efficient regulatory review and final approval by the regulatory agency
  - Timely access to the market to meet the needs, by expedient market launch

Human and Animal Health R&D Processes



Getting Novel Compounds to the Marketplace: The Discovery Process

Begins with a Target Profile

- Label Claim (treatment of X disease caused by X organisms)
- Market differentiators (single dose, oral, etc.)
  - Requires knowledge of current and future market conditions
- Market value

Key Points

- Investment is made at risk
- Timeline for process is 8–12 years

Getting Novel Compounds to the Marketplace: The Discovery Process

Preclinical Development Programs Identify Candidate Compounds

- Desirable efficacy including optimal ADME and PK parameters
- Favourable Animal Safety
- Demonstrable Human Food Safety
- Convenience of delivery system
- Positive Cost: Benefit ratio for the end-user

Getting Novel Compounds to the Marketplace: The Development Process

- Proof of efficacy: often not the rate-limiting step
- Greatest determining factors:
  - animal safety
  - method of delivery
  - economics
- Innovation can complicate PK / PD interpretation, may require new models
- Food animal compounds –
  - Complexity increases for food safety assessment
  - this increases development time and cost

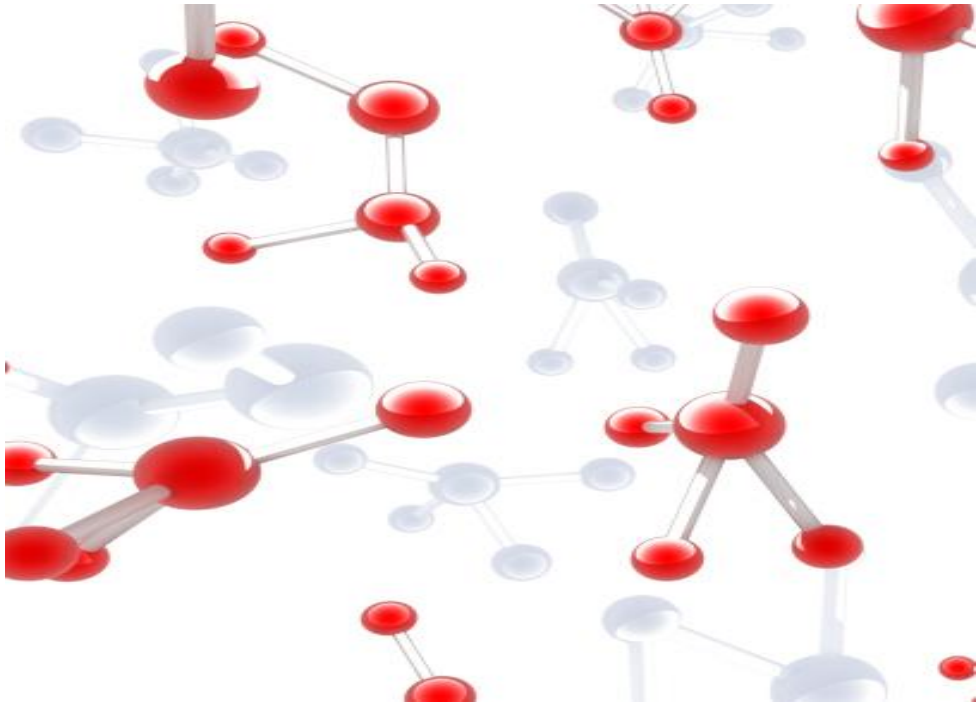
Getting Novel Compounds to the Marketplace: Manufacturing

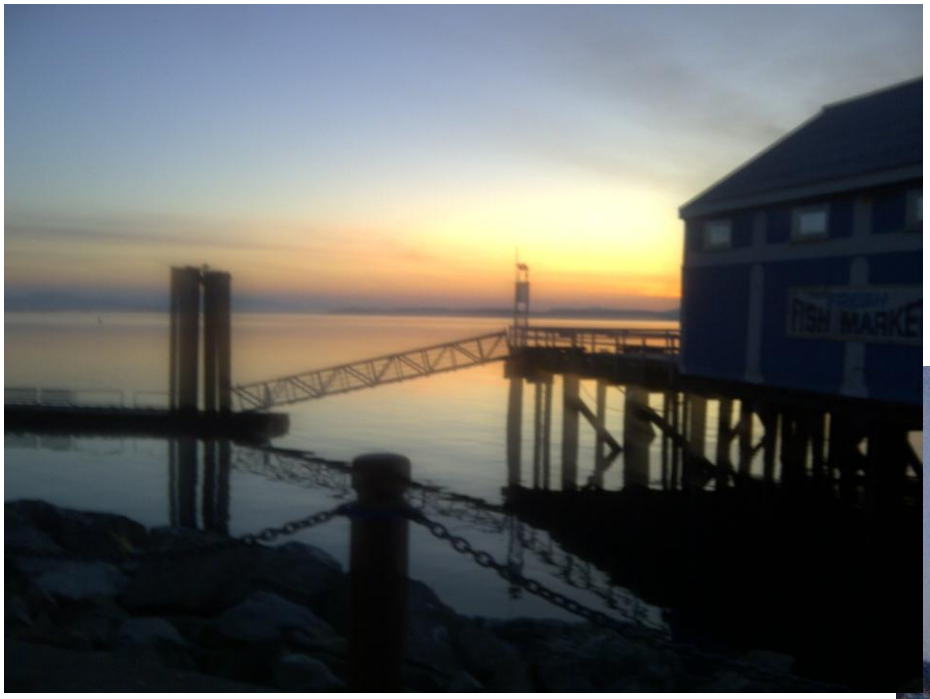
Manufacturing

- Ability to manufacture the product at sufficient scale is key to the commercial viability of the product
- COG calculations are critical to moving ahead
- GMP requirements and manufacturing facility restrictions can block the transition to full-scale production
- Oversight may vary by regulatory jurisdiction, making it difficult to align globally in GMP vs. non-GMP environments

Getting Novel Compounds to the Marketplace: Regulatory

- Novel Anti-infectives Must Meet the Regulatory Requirements of Traditional Small Molecules

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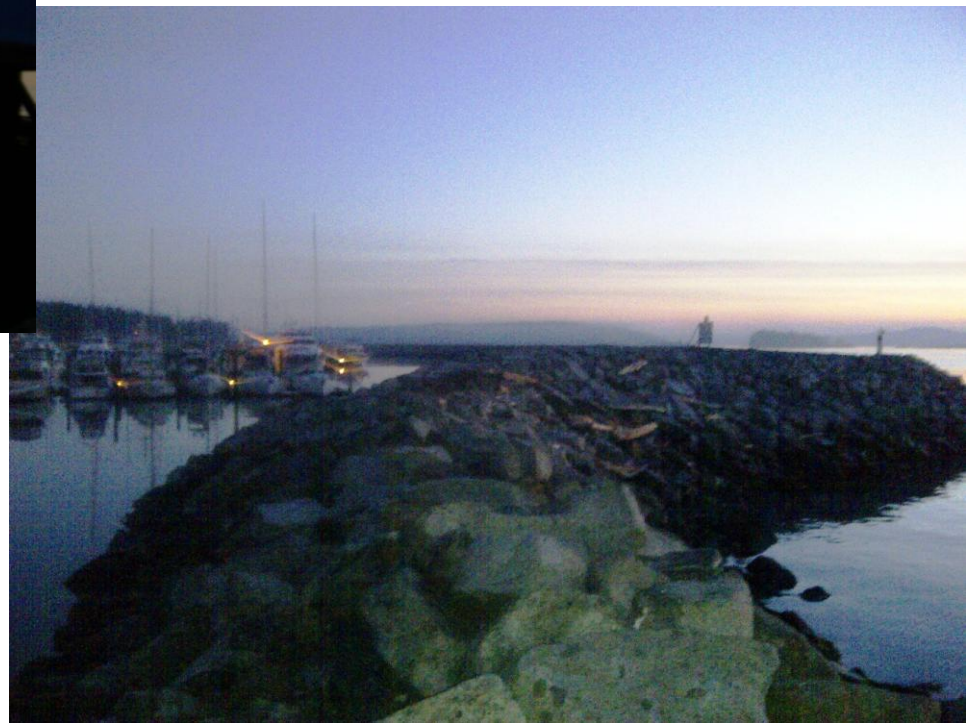


Courtesy City of Ottawa

Getting Novel Compounds to the Marketplace: Regulatory

Drug Substance

- ✓General Information
  - Nomenclature
  - Chemical Structure
  - Physicochemical Properties
- ✓Method of Manufacture
- ✓Structure Elucidation and Confirmation
- ✓Impurities
- ✓Control of the Drug Substance
- ✓Reference Standards
- ✓Packaging
- ✓Stability

Drug Product

- ✓Pharmaceutical Development
- ✓Method of Manufacture
- ✓Manufacturer(s)
- ✓Formulae
- ✓Quantitative formula
- ✓Batch formula
- ✓Manufacturing Process
  - Process Validation
  - Control of Excipients
  - Control of the drug product
- ✓Packaging
- ✓Stability
  - Accelerated & Long Term Studies
  - Proposed storage & shelf life

Getting Novel Compounds to the Marketplace: Regulatory

Efficacy

- ✓Microbiology
- ✓Laboratory *in-vitro*
- ✓Animal Model Efficacy
- ✓Clinical Pharmacology
- ✓Pharmacokinetics
- ✓Bioavailability
- ✓Pharmacodynamics
- ✓Dose determination
  - optimum dose & challenge
- ✓Dose confirmation
  - pivotal
  - clinical

Animal Safety

Laboratory Animal Studies

- ✓Acute Toxicity
- ✓Sub-chronic Toxicity
- ✓Chronic Toxicity
- ✓Irritation
- ✓Reproduction & Teratogenicity

Target Animal Safety Studies

- ✓Margin-of-Safety
- ✓Proposed Conditions of Use
- ✓Tissue Irritation
- ✓Reproductive Function
- ✓Clinical Safety
- ✓Pharmacovigilance Data

Getting Novel Compounds to the Marketplace: Regulatory

Human Food Safety

- ✓Laboratory Animal Studies
  - Acute, sub-chronic, chronic toxicity
  - Carcinogenicity, teratogenicity
  - Multigeneration reproductive
  - Genotoxicity
  - Pharmacological
  - Immunotoxicity,Neurotoxicity
- ✓Pharmacokinetics & Metabolism
- ✓Residue detection & depletion
- ✓NOEL & ADI
- ✓MRL & withdrawal period

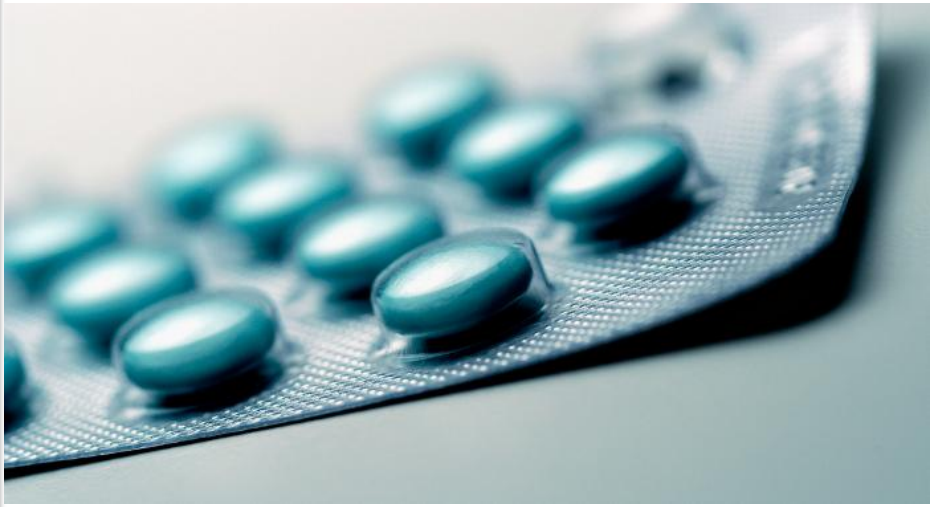
Microbial Safety

- ✓Resistance mechanism
- ✓Transfer of resistance genes
- ✓Cross-resistance
- ✓Co-resistance
- ✓Resistance development
- ✓Animal Gut Effect
- ✓Human Gut Effect
- ✓Impact on Human Medicine

Getting Novel Compounds to the Marketplace

Intellectual Property Protection

- Patent lifecycle is critical to return on R&D investment
- Maximization of IP protection hinges on efficient development, predictable regulatory review, and expedient access to the market



Conclusion: The Innovation Paradox

- Antibiotics are the only product category where increased use theoretically promotes more rapid obsolescence
- Contrary to popular belief, veterinarians don't have that many options for treating diseases
- Responsibly developing new antibiotics and alternatives to antimicrobials is important to both human and animal health and the regulatory pathway needs to remain predictable, transparent and science based
- Otherwise, Industry will invest R&D in other areas with the consequence that veterinarians will have even fewer treatment options available in the future – compromising our one health

Thank You!